IN THE CLAIMS

Please amend claims 1 and 14-16 as set forth below.

1. (Amended) A method for preparing porous microcrystalline cellulose granules comprising the following steps:

(a) granulating microcrystalline cellulose with a granulating fluid comprising water and a water-miscible, volatile, polar organic solvent to provide a granulated microcrystalline cellulose;

(b) drying the granulated microcrystalline cellulose at a controlled rate for a time sufficient to remove at least substantially all of the polar organic solvent from the granulated microcrystalline cellulose without removing at least a substantial portion of the water from the granulated microcrystalline cellulose, and without extruding or spheronizing the granulated microcrystalline cellulose from granulation step (a); and

(c) subsequent to step (b), removing at least a substantial portion of the water from the granulated microcrystalline cellulose.

14. Porous, granulated microcrystalline cellulose made by the process of claim 1 having a loose bulk density of from about 0.2 g/cc to about 0.4 g/cc, and a mean particle size of from about 250 microns to about 1500 microns.

15. Porous, granulated microcrystalline cellulose made by the process of claim 7 having a loose bulk density of from about 0.2 g/cc to about 0.4 g/cc, and a mean particle size of from about 250 microns to about 1500 microns.

16. Porous microcrystalline cellulose granules having an irregular shape, a loose bulk density of from about 0.2 g/cc to about 0.4 g/cc, and a mean particle size of from about 250 microns to about 1500 microns.

REMARKS

Claims 1 and 14-16 have been amended. Claims 1-26 are currently pending in the present application.

The present invention relates to a method for making porous microcrystalline cellulose granules by granulating microcrystalline cellulose with a combination of water and a water-miscible, volatile, polar organic solvent. After granulation, the granules are first dried to remove substantially all of the polar organic solvent without removing a substantial portion of the water and without spheronizing or extruding the granules. Subsequent to removing substantially all of the polar organic solvent, a substantial portion of the water is removed from the granules to thereby obtain the porous microcrystalline cellulose granules. This granulation process produces a special form of microcrystalline cellulose granules that are characterized by a large mean particle size (i.e. 250-1000 microns), and a relatively high porosity (i.e. loose bulk density of 0.2-0.4g/cc). The examples of the present application demonstrate that these microcrystalline cellulose granules provide an enhanced cushioning effect compared to similar, commercially available microcrystalline cellulose granules whereby these granules of microcrystalline cellulose can be employed to protect controlled-release particles contained in pharmaceutical formulations during, for example, tabletting operations.

Claims 14-16 and 20-26 have been rejected under 35 U.S.C. §102(e) as being anticipated by U.S. Patent No. 6,149,943 (McTeigue et al.). This rejection, at least insofar as it applies to claims 14-16 and 20-26, as amended, is respectfully traversed and reconsideration is requested for the reasons, which follow.

McTeigue et al. discloses microcrystalline cellulose particles having an average particle size of 160-220 microns (col. 1, line 54) and a tapped bulk density of 0.40-0.45 g/cc (col. 2, lines 51-52). Claims 14-16 have been amended to require "porous" microcrystalline cellulose granules having a mean particle size of at least 250 microns. McTeigue et al. does not disclose microcrystalline cellulose granules having a mean particle size of at least 250 microns and thus independent claims 14 and 16 are

considered to be novel over McTeigue et al. for at least this reason. All of claims 20-26 depend from claim 16 and thus are considered novel for at least the same reasons as for claim 16.

The compositions of claims 14-16 and 20-26 are also considered to be unobvious over McTeigue et al. since McTeigue et al. does not teach the granules, as claimed, McTeigue et al. does not disclose a process for obtaining such granules, and because the granules of the present invention exhibit significant, unexpected results in the form of the enhanced cushioning properties demonstrated in the examples of the present application. Favorable consideration and withdrawal of the rejection of claims 14-16 and 20-26 over McTeigue et al. is requested.

Claims 14-17 and 20-26 have been rejected under 35 U.S.C. §102(e) as being anticipated by U.S. Patent No. 6,117,451 (Kumar). This rejection, at least insofar as it applies to claims 14-17 and 20-26, as amended, is respectfully traversed and reconsideration is requested for the reasons, which follow.

Kumar discloses microcrystalline cellulose that has a particle size range of 150-220 microns and a density range of 0.20-0.45 g/ml (col. 9, lines 21-23). Claims 14-16, as amended, require porous microcrystalline cellulose granules having a mean particle size of at least 250 microns. Thus, claims 14-16, as amended, are considered to be clearly novel over Kumar. Claims 17 and 20-26 all depend from claim 16 and thus these claims are considered to be novel over Kumar for at least the same reason as given for claim 16.

The compositions of claims 14-17 and 20-26 are also considered to be unobvious over Kumar since Kumar does not teach the granules, as claimed, Kumar does not disclose a process for obtaining such granules, and because the granules of the present invention exhibit significant, unexpected results in the form of the enhanced cushioning properties demonstrated in the examples of the present application. Favorable consideration and withdrawal of the rejection of claims 14-17 and 20-26 over Kumar is requested.

Claims 1-13 have been rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 6,123,964 (Asgharnejad et al.) in view of U.S. Patent No. 5,725,886 (Erkoboni et al.). This rejection, at least insofar as it applies to claims 1-13, as amended, is respectfully traversed and reconsideration is requested for the reasons, which follow.

The Examiner takes the position that,

> "The Asgharnejad et al patent discloses a process comprising the steps that involves (1) forming a powder blend of the active ingredient with a binder/diluent, a first diluent, a second diluent, and a disintegrant, using a mixer; (2) wet granulating the powder blend by adding a solution of ethanol/water to the powder blend; (3) drying the granules to remove the ethanol/water with heated air in a fluidized bed dryer or tray dryer (see column 2, line 63 to column 3, line 6)."

Claims 1-13, as amended, require a two-step drying process that is neither taught nor suggested in Asgharnejad et al. In the first step of this two-step drying process, substantially all of the polar organic solvent is removed from the microcrystalline cellulose granules without removing a substantial portion of the water from the granules. In the second step, after substantially all of the polar organic solvent has been removed, a substantial portion of the water is removed. This two-step drying process provides a novel porous microcrystalline cellulose product that exhibits enhanced cushioning properties for cushioning controlled-release particles during tabletting, as is demonstrated in the examples of the present application.

Asgharnejad et al. does not disclose a two step drying process, but instead discloses a single step of drying to remove the ethanol/water with heated air in a fluid bed dryer or tray dryer for 10 minutes to 24 hours. Thus, the process of Asgharnejad et al. is distinguishable from the process of claims 1-13 of the present application, as amended, for at least this reason. Asgharnejad et al. also does not teach or suggest carrying out the drying step in two stages as in the present invention nor does Asgharnejad et al. give a skilled person any reason to believe that a two step drying process would be beneficial.

The Examiner relies on Erkoboni et al. as disclosing compositions containing a combination of microcrystalline cellulose and hydrocolloids, presumably in relation to claim 7 of the present application. Erkoboni et al. does not disclose the use of the two-step drying process of the present invention and thus does not cure the deficiency of Asgharnejad et al. Accordingly, favorable consideration and withdrawal of the rejection of claims 1-13, as amended, is requested.

Claims 14-26 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Kumar in view of U.S. Patent No. 5,384,130 (Kamada). This rejection, at least insofar as it applies to claims 14-26, as amended, is respectfully traversed and reconsideration is requested for the reasons, which follow.

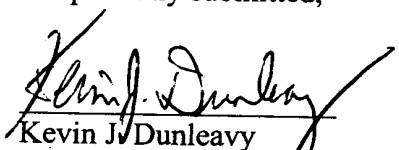
Kumar discloses microcrystalline cellulose that has a particle size range of 150-220 microns and a density range of 0.20-0.45 g/ml (col. 9, lines 21-23). The Examiner concedes that claims 14-26 differ from Kumar in that these claims, as amended, require microcrystalline cellulose granules having particle sizes of from 250-1000 microns. The Examiner relies on Kamada to show that microcrystalline cellulose granules having particle sizes within the range of 250-1000 microns are known in the art and thus concludes that it would have been obvious to modify the pharmaceutical preparation of the Kumar patent by substituting for the microcrystalline cellulose thereof, a microcrystalline cellulose that has a particle size of 100-1000 microns as disclosed in Kamada since the Kamada suggests that such microcrystalline cellulose allows for improved stability of the active ingredients.

However, substitution of the microcrystalline cellulose of Kamada for the microcrystalline cellulose of Kumar does not result in a composition as claimed in any of claims 14-26 since the microcrystalline cellulose of Kamada is spherical (see col. 2, lines 42-49 of Kamada) and the microcrystalline cellulose of Kamada must have a tapped bulk density of at least 0.65 g/ml (see col. 4, line 3 of Kamada). Claims 14-26 require that the loose bulk density should be 0.2-0.4 g/cc which is significantly lower than the bulk density required by Kamada. Claims 14-15 are directed to non-

spherical granules since claim 1 excludes the use of spheronizing in the granulation process. Claims 16-26 all require microcrystalline cellulose granules having an irregular shape and thus these granules are also non-spherical. Thus, even if it were obvious to combine the teachings of Kamada with the teachings of Kumar as the Examiner suggests, one would not arrive at the present invention as claimed in claims 14-26. Withdrawal of the rejection of claims 14-26 over Kumar in view of Kamada is requested.

Favorable consideration and issuance of a notice of allowance are solicited.

Respectfully submitted,



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